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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,104	02/10/2005	Birkir Sveinsson	3535-0138PUS1	3834
2292 7590 08/30/2007 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			EXAMINER WEN, SHARON X	
			ART UNIT 1644	PAPER NUMBER
			NOTIFICATION DATE 08/30/2007	DELIVERY MODE ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

# Office Action Summary

Application No.

10/524,104

Applicant(s)

SVEINSSON, BIRKIR

Examiner

Sharon Wen

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 17 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 9-14 is/are pending in the application.
- 4a) Of the above claim(s) 4 and 9-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet</u>             |

**Continuation of Attachment(s) 6). Other: Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.**

### DETAILED ACTION

1. The Art Unit location of the examiner of this application in the PTO has changed. To aid in the correlating any papers for this application, all further correspondence regarding this application should be directed to Sharon Wen, Group Art Unit **1644**, Technology Center 1600.

#### *Election/Restrictions*

2. Applicant's election with traverse of Group I and species "CGRP derivatives including the peptide CGRP 8-37" and topical administration in the Response to Election/Restriction filed on 07/17/2007 is acknowledged. The traverse is on the ground that the Breton reference (U.S. Patent 5,851,556) cited in the Restriction Requirement does not suggest or disclose an associated of CGRP with psoriasis. This is not found to be persuasive for reasons of record set forth in the Restriction Requirement mailed 07/17/2007. The reference teach an invention for preventing and or combating pruritus, which is associated with *psoriasis* comprising topical administration of an antagonist of *CGRP* (see column 3, lines 61-64; column 5, lines 33-38; column 8, lines 56-57; column 9 lines 11-13 and 19-21).

The requirement is still deemed proper and is therefore made FINAL.

Upon further consideration, examination has been extended to include "dermally" as recited in claim 3.

3. Claim 6-8 has been canceled.

Claims 1-5 and 9-14 are pending.

Claims 4 and 9-14 have been withdrawn from further consideration under 37 CFR § 1.142(b) as being drawn to non-elected Inventions.

Claims 1-3 and 5 are currently under examination as they read on a method of treating, remedying or preventing psoriasis comprising administering CGRP derivatives including the peptide CGRP 8-37 as the claimed invention.

***Priority***

4. The effective priority date for claims 17, 19, 21-22 and 28 are deemed to be the filing date PCT/IS03/00023, i.e. **08/12/2003**.

Applicant is invited to amend the first line of the specification to reflect Applicant's claim for priority.

***Information Disclosure Statement***

5. Applicant's IDSs, filed on 02/10/2005, 12/01/2005 and 09/07/2006 are acknowledged, and have been considered.

***Sequence Compliance***

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825 (see specification on page 10, lines 28-29). However, this application fails to comply with the requirements set forth on the attached **Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures**.

Applicant is required to fulfill these requirements.

***Applicant must comply with the requirements of the sequence rules (37 CFR 1.821-1.825 in response to this Office Action.***

***Specification***

7. Applicant is requested to review the application for the use of trademarks, embedded hyperlinks and/or other form of browser-executable code (e.g. see page 4 line 20 of specification).

Trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference.

***Claim Rejections - 35 USC § 112 second paragraph***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding the instant claims, the phrases “including” and “such as” render the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Applicant is invited to amend the claims to proper Markush format and avoid the recitation of “such as” and “including”.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any New Matter. See MPEP § 714.02 and 2163.06.

***Claim Rejections - 35 USC § 112 first paragraph***

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 1-3 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the **written description** requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C § 112, paragraph 1 "Written Description" requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January, 2001, See especially page 1106 3<sup>rd</sup> column).

The instant claims are directed to a method of treating, remedying or preventing psoriasis comprising administering at least one CGRP antagonist compound that is a CGRP **derivative**. Regarding the instant claim limitations, the specification does not appear to provide an adequate written description for the genus of CGRP derivatives encompassed in the claim.

The present claims recite a genus of CGRP derivatives which read on any modification of the CGRP polypeptide including homologs, fragments and amino acid substitution. However the instant specification discloses only one CGRP derivative, i.e. CGRP 8-37, a fragment resulted from tryptase cleavage of CGRP polypeptide, which is a high affinity antagonist for the CGRP receptor.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, Burgess et al (J Cell Biol. 111:2129-2138, 1990) show that a conservative replacement of a single "lysine" residue at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similarly, Lazar et al. (Mol Cell Biol. 8:1247-1252, 1988) teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

In the absence of sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, the claimed invention is not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of all CGRP derivatives that would inhibit receptor binding of CGRP.

For the above reasons, it is clear that Applicant does not have possession of all the possible CGRP derivatives at the time the application was filed. As such, the instant claims are rejected for failure to comply with the written description requirement under 35 U.S.C. 112 first paragraph.

*Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116.) Consequently, Applicant was not in possession of the instant claimed invention. See *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision. (See page 1115.)

12. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the **enablement** requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.



The instant claims are rejected for the recitation of “preventing”. In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of immunosuppressive drugs or biopharmaceutical drugs can be species- and model-dependent, it is not clear that reliance on the in vitro and in vivo experimental observations as well as the clinical experience with targeting a disorder resulting from release of CGRP with an antagonist of CGRP accurately reflects the relative ability or efficacy of the claimed methods to prevent psoriasis wherein the CGRP antagonist compound blocks binding of CGRP to its receptors is therapeutically beneficial.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of *Ex parte Aggarwal*, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

The specification does not adequately teach how to effectively prevent psoriasis or reach an appropriate beneficial therapeutic endpoint in humans by administering a CGRP antagonist. The specification does not teach how to extrapolate data obtained from various in vitro observations as well as clinical experience with a CGRP antagonist to the development of effective methods of preventing the disorder broadly encompassed by the claimed invention (page 7, lines 5-13).

Also, it is noted that experimental protocols usually are conducted under defined conditions wherein the antagonist and the stimulus / insult occur at the same or nearly the same time. Immunosuppression is much easier to achieve under such controlled conditions that experienced in the human disorders or diseases such as the psoriasis-like hyperproliferation, increased number of T-cells, increase blood flow, and localization of lesions targeted by the claimed invention (see page 7 lines 30-32 of the instant specification). With respect to in vivo studies, animal models validate concepts based on studies of human disease; such studies are limited to the "acute" as opposed to "chronic" nature of the disease. In animal models, the onset of the pathological phenomena listed above is rapid with an aggressive destructive process, whereas in humans the disease progresses more slowly, often with natural periods of disease exacerbation and remission. Generally, such diseases are diagnosed only after significant tissue damage has occurred.

There is insufficient guidance and direction as well as objective evidence to provide for preventing the diversity and scope of diseases encompassed by the claimed methods.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective methods to prevent psoriasis, undue experimentation would be required to practice the claimed method of preventing psoriasis with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for preventing the diseases or disorders encompassed by the claimed methods and products.

Applicant is invited to amend the claims to avoid the recitation of "preventing".

### ***Claim Rejections - 35 USC § 102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1644

14. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Brenton et al. (U.S. Patent 6,019,967, see entire document).

Brenton et al. teach a method of treating psoriasis comprising administering topically or dermally CGRP 8-37 (e.g., see Abstract and column 4, in particular, line 44).

### *Conclusion*

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Wen whose telephone number is (571) 270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

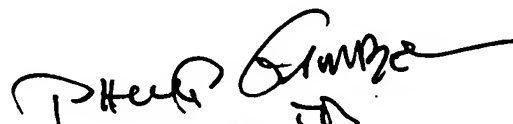
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Wen Ph.D.

Patent Examiner

August 17, 2007

  
PHILLIP GAMBEL, PH.D  
PRIMARY EXAMINER  
TZ-1600  
8/16/07

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING  
NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 CFR 1.821 - 1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).
- ☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).
- ☐ 7.

Other: \_\_\_\_\_

**Applicant must provide:**

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing"
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d)

For questions regarding compliance with these requirements, please contact:

For Rules Interpretation, call (703) 308-1123

For CRF submission help, call (703) 308-4212

For PatentIn software help, call (703) 557-0400

Please return a copy of this notice with your response.